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<p>(21) International Application Number: PCT/US97/21437</p> <p>(22) International Filing Date: 26 November 1997 (26.11.97)</p> <p>(30) Priority Data: 60/031,607 27 November 1996 (27.11.96) US</p> <p>(71) Applicants: THE GENERAL HOSPITAL CORPORATION [US/US]; 55 Fruit Street, Boston, MA 02114 (US). BRANDEIS UNIVERSITY [-/US]; P.O. Box 9110, Waltham, MA 02254-9110 (US).</p> <p>(72) Inventors: ISRAEL, Esther, Jacobowitz; 19 Alden Street, Newton, MA 02159 (US). SIMISTER, Neil, E.; 415 South Street, Waltham, MA 02254 (US).</p> <p>(74) Agent: FRASER, Janis, K.; Fish & Richardson, P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).</p>		<p>(81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: MODULATION OF IgG BINDING TO FcRn</p> <p>(57) Abstract</p> <p>Disclosed are mutant IgG molecules having altered amino acid sequences in the FcRn-binding region. These changes confere increased or decreased affinity for FcRn and thus, respectively, a decreased or increased rate of clearance from the systemic circulation. Such molecules can be attached to detectable labels or cytotoxic moieties for imaging tissues or for delivering cytotoxins. Also disclosed is a method for identifying IgG molecules with altered half-lives in circulation by contacting the molecules with FcRn.</p> <p><i>These studies use mouse</i></p>		

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mIgG1	248		*					257	
	<u>Lys</u>	Asp	<u>Val</u>	<u>Leu</u>	<u>Thr</u>	<u>Ile</u>	<u>Thr</u>	<u>Leu</u>	<u>Thr</u>
			<u>Thr</u>		<u>Leu</u>		<u>Val</u>		
									(SEQ ID NO: 1)
mIgG1	308		*	*				314	
	<u>Ile</u>	<u>Met</u>	<u>His</u>	<u>Gln</u>	Asp	Trp	<u>Leu</u>		(SEQ ID NO: 2)
mIgG1	429				*	*		436	
	<u>His</u>	<u>Glu</u>	<u>Gly</u>	<u>Leu</u>	<u>His</u>	<u>Asn</u>	<u>His</u>	<u>His</u>	(SEQ ID NO: 3)
mIgG2a	248							257	
	<u>Lys</u>	Asp	<u>Val</u>	<u>Leu</u>	<u>Met</u>	<u>Ile</u>	<u>Ser</u>	<u>Leu</u>	<u>Ser</u>
		<u>Asn</u>							(SEQ ID NO: 4)
mIgG2a	308							314	
	<u>Ile</u>	<u>Gln</u>	<u>His</u>	<u>Gln</u>	Asp	Trp	<u>Met</u>		(SEQ ID NO: 5)
mIgG2a	429							436	
	<u>His</u>	<u>Glu</u>	<u>Gly</u>	<u>Leu</u>	<u>His</u>	<u>Asn</u>	<u>His</u>	<u>Leu</u>	(SEQ ID NO: 6)
			<u>Val</u>					<u>His</u>	
mIgG2b	248							257	
	<u>Lys</u>	Asp	<u>Val</u>	<u>Leu</u>	<u>Met</u>	<u>Ile</u>	<u>Ser</u>	<u>Leu</u>	<u>Thr</u>
								<u>Ser</u>	<u>Pro</u>
									(SEQ ID NO: 7)
mIgG2b	308							314	
	<u>Ile</u>	<u>Gln</u>	<u>His</u>	<u>Gln</u>	Asp	Trp	<u>Met</u>		(SEQ ID NO: 8)
mIgG2b	429							436	
	<u>His</u>	<u>Glu</u>	<u>Gly</u>	<u>Leu</u>	<u>Lys</u>	<u>Asn</u>	<u>Tyr</u>	<u>Tyr</u>	(SEQ ID NO: 9)
mIgG3	248							257	
	<u>Lys</u>	Asp	<u>Ala</u>	<u>Leu</u>	<u>Met</u>	<u>Ile</u>	<u>Ser</u>	<u>Leu</u>	<u>Thr</u>
								<u>Pro</u>	
									(SEQ ID NO: 10)
mIgG3	308							314	
	<u>Ile</u>	<u>Gln</u>	<u>His</u>	<u>Gln</u>	Asp	Trp	<u>Met</u>		(SEQ ID NO: 11)
mIgG3	429							436	
	<u>His</u>	<u>Glu</u>	<u>Ala</u>	<u>Leu</u>	<u>His</u>	<u>Asn</u>	<u>His</u>	<u>His</u>	(SEQ ID NO: 12)

FIG. 2A